

Remarks

Support for the Amendments

Support for the amendments to claims 52, 61-63 and 69, and for new claims 70-78 can be found throughout the present specification. Specifically, support for the amendment to claim 52 can be found throughout pages 31-35 and throughout the Examples. Support for the amendments claim 69, and for new claims 70-78, can be found throughout pages 22-23 and 31-46. The amendments to claims 61-63 are sought to provide the proper dependency for these claims upon cancellation of claim 60. Therefore, these amendments do not add new matter and their entry and consideration are respectfully requested.

Status of the Claims

By the foregoing amendments, claims 52, 61-63 and 69 are sought to be amended, and new claims 70-78 are sought to be added. Claim 60 has been canceled without prejudice or disclaimer thereto. Upon entry of the foregoing amendments, claims 52-59 and 61-78 are pending in the application, with claims 52, 69, 71 and 75 being the independent claims.

Summary of the Office Action

In the Office Action dated October 1, 2004, the Examiner has made two rejections of, and one objection to, the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and objections and that they be withdrawn.

The Rejection Under 35 U.S.C. § 102(b) Over Bebee

In the Office Action at pages 3-6, the Examiner has rejected claims 52-63 and 66-69 under 35 U.S.C. § 102 (b), as being anticipated by Bebee *et al.*, U.S. Patent No. 5,434,066 (hereinafter "Bebee"). By the foregoing amendments, claim 60 has been canceled without prejudice or disclaimer. Hence, the portion of this rejection that may have applied to this claim has been rendered moot. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

The Examiner states that Bebee discloses the generation of different vectors where desired sequences were obtained from the phage P1 genome via PCR amplification. The Examiner contends that Bebee discloses an example where "the 'recombination protein' is the ligase used to join a linear fragment of DNA comprising adapters at either terminus that in turn comprise 'at least a portion of' a recombination site (e.g. any dinucleotide sequence found in any given recombination site) with a vector nucleic acid in an *in vitro* reaction mixture." Office Action at page 4, second full paragraph, lines 7-9. The Examiner therefore concludes that Bebee discloses the presently claimed invention. Applicants respectfully disagree with this conclusion.

Present claim 52 (and hence claims 53-59, 61-63 and 66-68 that depend ultimately therefrom and that are also rejected over Bebee) recites an *in vitro* method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites, the method comprising: obtaining at least one isolated linear nucleic acid molecule; contacting the molecule *in vitro* with one or more adapters which comprise at least a first recombination site or portions thereof under conditions sufficient to add one or more of the adapters to one or more termini of the linear nucleic acid molecule; and mixing the linear nucleic acid

molecule with at least one vector, comprising at least a second recombination site or portions thereof, *in vitro* in the presence of at least one recombination protein, under conditions sufficient to cause recombination between the first and second recombination sites.

Present claim 69 recites an *in vitro* method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites, the method comprising: obtaining at least one isolated linear nucleic acid molecule; and contacting the molecule *in vitro* with one or more adapters which comprise at least a first recombination site or portions thereof under conditions sufficient to add one or more of the adapters to one or more termini of the linear nucleic acid molecule, wherein the at least first recombination site or portions thereof are *att* sites or mutants or variants thereof.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). Applicants respectfully submit that Bebee does not disclose every element of present claim 52 or present claim 69 (and hence the dependent claims noted above), and therefore cannot anticipate the presently claimed invention.

As discussed in the previous reply, filed June 24, 2004 (incorporated by reference herein in its entirety), Applicants respectfully submit that Bebee does not disclose the *in vitro* methods of the presently claimed invention, being limited instead to *in vivo* recombination wherein the recombination takes place inside of host cells (*see, e.g.*, Bebee in the title; in the abstract; at column 2, lines 47-55; at column 3, lines 46-58; in Example 2, at column 12, lines 16-20; and in Example 5, at columns 17-20). Hence, for at least this reason, Bebee does not anticipate the presently claimed invention.

The Examiner states that "[t]he specification of the '066 patent does not make clear that the Cre-mediated recombination took place *in vitro* or *in vivo*." Office Action at page 5, second full paragraph, lines 4-5. Applicants respectfully disagree with this statement. Applicants submit that, while Bebee discloses the treatment of the resultant plasmid with the Cre recombination protein *in vitro*, it is not until this plasmid is "transformed *into E. coli* cells" (emphasis added) that the recombination reaction occurs and the pZL plasmid is generated. *See* Bebee at column 12, lines 58-62. Therefore, Bebee does not disclose the *in vitro* methods of the present invention. Hence, in view of *Kalman*, Bebee cannot and does not anticipate the presently claimed invention.

The Examiner concedes that the generation of the pZL plasmid disclosed in Bebee "was not via the recited method and this was never the examiner's contention." Office Action at page 5, second full paragraph, lines 5-7. The Examiner contends that "[r]ather, given the broad definitions provided by the instant specification and the wording of the instant claims, the examiner has interpreted the claim language broadly as encompassing any embodiment wherein a linear DNA is incorporated (i.e. 'recombined') into a vector to generate a recombinant DNA molecule comprising the linear DNA." Office Action at page 5, second full paragraph, lines 7-11. Applicants respectfully disagree with these contentions.

Applicants submit that the Examiner's interpretation of the term "recombination site" is inconsistent with both the present specification and the ordinary meaning of this term. Applicants respectfully submit that the skilled artisan, guided by ordinary skill in the art as well as the present specification, would readily understand that the term "recombination site" refers to a site-specific recombination site that is acted upon by a recombination protein during a recombination reaction. Applicants respectfully submit that Bebee does not

disclose all of the elements of the present claim 52, specifically the *in vitro* recombination between the first and second recombination sites as recited in this claim. Applicants further submit that the Examiner has not provided any reference which discloses all of the elements of present claim 52 (and hence the dependent claims noted above).

With regard to present claim 69, Applicants respectfully submit that Bebee does not disclose contacting a nucleic acid molecule *in vitro* with one or more adapters which comprise at least a first recombination site or portions thereof under conditions sufficient to add one or more of the adapters to the nucleic acid molecule, wherein the at least first recombination site or portions thereof are *att* sites or mutants or variants thereof. Hence, Bebee does not disclose all of the elements of present claim 69, and therefore, in view of *Kalman*, Bebee cannot and does not anticipate the presently claimed invention. Applicants further submit that Bebee does not disclose all of the elements of new claims 70-78, and hence, these claims are allowable over Bebee.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 52-59, 61-63 and 66-69 under 35 U.S.C. § 102(e) over Bebee.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 6, the Examiner has rejected claims 52-69 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. By the foregoing amendments, claim 60 has been canceled without prejudice or disclaimer.

Hence, the portion of this rejection that may have applied to this claim has been rendered moot. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

The Examiner contends that the nature of the "conditions sufficient to cause recombination of said linear nucleic acid molecule with said vector" recited in claim 52 is unclear. The Examiner further contends that the claim encompasses embodiments wherein the recombination reaction between the vector and linear nucleic acid is not mediated by the recombination protein. Applicants respectfully disagree with these contentions.

Present claim 52 (and hence the dependent claims noted above) recites mixing the linear nucleic acid molecule with at least one vector, comprising at least a second recombination site or portions thereof *in vitro* in the presence of at least one recombination protein, under conditions sufficient to cause recombination between the first and second recombination sites. Applicants respectfully submit that the ordinarily skilled artisan would readily recognize that the recited method requires the interaction between the recombination site(s) on the linear nucleic acid molecule and the recombination site(s) on the vector, in the presence of a recombination protein, such that a recombination reaction occurs between the recombination sites. Applicants further submit that "conditions sufficient to cause recombination" are well known to those skilled in the art, particularly in view of the significant detailed disclosure of such conditions provided in the present specification (*see e.g.*, Examples 1-12). Applicants respectfully submit that the present specification provides sufficient disclosure of such conditions, and hence, the metes and bounds of these conditions are clearly set forth.

Applicants further note that the "conditions sufficient to add one or more of the adapters to one or more termini of the linear nucleic acid molecule" as recited in present

claim 69 are also well known in the art. Furthermore, such conditions are clearly set forth in the present specification (*see e.g.*, specification at page 29, lines 5-30; and throughout Examples 1-12). Applicants therefore respectfully submit that this phrase is neither vague nor indefinite, and the metes and bounds of these conditions are clearly set forth in the present specification.

In view of the foregoing remarks, Applicants respectfully request that the rejection of claims 52-59 and 61-69, under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

The Objection to Claim 64

In the Office Action at page 7, the Examiner has objected to claim 64, indicating that this claim would be free of the cited art if rewritten in independent form comprising each of the limitations of the claim upon which it is currently dependent. Applicants thank the Examiner for identification of this provisionally allowable subject matter. However, in view of the foregoing remarks, Applicants respectfully submit that all of the present claims are allowable. Hence, reconsideration and withdrawal of this objection are respectfully requested.

Conclusion

All of the stated grounds of rejection and objection have been properly traversed, rendered moot, or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn, and that all pending claims be allowed.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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